



Quirk, Helen and Blake, Holly and Tennyson, R. and Randell, T.L. and Glazebrook, C. (2014) Physical activity interventions in children and young people with Type 1 diabetes mellitus: a systematic review with meta-analysis. *Diabetic Medicine*, 31 (10). pp. 1163-1173. ISSN 1464-5491

Access from the University of Nottingham repository:

<http://eprints.nottingham.ac.uk/38997/1/dme0031-1163.pdf>

Copyright and reuse:

The Nottingham ePrints service makes this work by researchers of the University of Nottingham available open access under the following conditions.

This article is made available under the Creative Commons Attribution Non-commercial licence and may be reused according to the conditions of the licence. For more details see: <http://creativecommons.org/licenses/by-nc/2.5/>

A note on versions:

The version presented here may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher's version. Please see the repository url above for details on accessing the published version and note that access may require a subscription.

For more information, please contact eprints@nottingham.ac.uk

Systematic Review or Meta-analysis

Physical activity interventions in children and young people with Type 1 diabetes mellitus: a systematic review with meta-analysis

H. Quirk¹, H. Blake¹, R. Tennyson¹, T. L. Randell² and C. Glazebrook³

¹School of Health Sciences, University of Nottingham, ²Department of Paediatric Endocrinology and Diabetes, Nottingham Children's Hospital and ³Division of Psychiatry and Applied Psychology, University of Nottingham, Nottingham, UK

Accepted 20 June 2014

Abstract

Aims To synthesize evidence from randomized and non-randomized studies of physical activity interventions in children and young people with Type 1 diabetes so as to explore clinically relevant health outcomes and inform the promotion of physical activity.

Method We conducted a search of CINAHL Plus, the Cochrane Library, EMBASE, MEDLINE, PsycINFO, SCOPUS, SportDiscus and Web of Science between October and December 2012. Eligible articles included subjects aged ≤ 18 years with Type 1 diabetes and a physical activity intervention that was more than a one-off activity session. Physiological, psychological, behavioural or social outcomes were those of interest.

Results A total of 26 articles (10 randomized and 16 non-randomized studies), published in the period 1964–2012, were reviewed. Although there was heterogeneity in study design, methods and reporting, 23 articles reported at least one significant beneficial health outcome at follow-up. Meta-analyses of these studies showed potential benefits of physical activity on HbA_{1c} (11 studies, 345 participants, standardized mean difference -0.52, 95% CI -0.97 to -0.07; $P = 0.02$), BMI (four studies, 195 participants, standardized mean difference -0.41, 95% CI -0.70 to -0.12; $P = 0.006$) and triglycerides (five studies, 206 participants, standardized mean difference -0.70, 95% CI -1.25 to -0.14; $P = 0.01$). The largest effect size was for total cholesterol (five studies, 206 participants, standardized mean difference -0.91, 95% CI -1.66 to -0.17; $P = 0.02$).

Conclusions Physical activity is important for diabetes management and has the potential to delay cardiovascular disease, but there is a lack of studies that are underpinned by psychological behaviour change theory, promoting sustained physical activity and exploring psychological outcomes. There remains a lack of knowledge of how to promote physical activity in people with Type 1 diabetes.

Diabet. Med. 31, 1163–1173 (2014)

Introduction

People with Type 1 diabetes have at least twice the risk of developing cardiovascular disease compared with those without diabetes [1]. In people with diabetes, cardiovascular disease risk factors, such as endothelial dysfunction, can present as early as preadolescence [2]; therefore, young people with Type 1 diabetes are advised to engage in regular

physical activity, with appropriate insulin and dietary adjustments [3], and the promotion of life-long physical activity in young people with Type 1 diabetes is a priority.

UK government guidelines recommend that children and young people perform at least 60 min of moderate-to-vigorous physical activity daily, including muscle and bone strengthening activities, on at least 3 days of the week [4]. In young people, this level of physical activity improves cardiovascular health, maintains healthy weight, improves bone health, improves self-confidence and develops new social skills [4]. Although the benefits of physical activity for psychological health are well established, there has been little exploration of its potential psychological impact for those with Type 1 diabetes. Young people with Type 1 diabetes are

Correspondence to: Cris Glazebrook.
E-mail: cris.glazebrook@nottingham.ac.uk

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

prescribed physical activity as part of diabetes management and so might have a unique perception of being physically active and thus a unique psychological experience [5].

The importance of physical activity for young people is reinforced by public health authorities and government guidelines [6]. Nevertheless, figures show that levels of physical activity [7], including among young people with Type 1 diabetes [8], are insufficient to accrue the associated health benefits, and young people with diabetes may be less active than those without diabetes [9,10]. This increases the existing risk of cardiovascular disease for young people with diabetes and emphasizes the need to promote physical activity in this population. Evidence in other populations, including in those with Type 2 diabetes, suggests that physical activity promotion strategies based on theoretical models of behaviour change are more likely to result in sustained physical activity [11].

Until recently, no systematic review evidence of physical activity interventions for young people with Type 1 diabetes had been published. In 2014, MacMillan *et al.* [12] reviewed randomized controlled trials and, in 2013, Kennedy *et al.* published a review with a focus on glycaemic control [13]. The present review is unique as it synthesizes the results of both non-randomized and randomized trials and thus covers a wider range of studies and outcomes. Valuable insights can be gleaned from including non-randomized trials, provided that attention is paid to the risk of confounders and heightened bias [14]. This inclusivity enables evaluation of the strengths and limitations of interventions, which can inform future physical activity promotion. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for the planning, conduct and report of this review.

The aims of the present review were as follows: to examine a range of clinically relevant health outcomes of physical activity interventions; to examine the characteristics of existing interventions, including adherence rates and adverse events; and to recommend physical activity promotion strategies.

Methods

Study eligibility

Studies eligible for inclusion in the present review included only those with study populations of children and young people aged ≤ 18 years, clinically diagnosed with Type 1 diabetes. Study interventions were physical activity, which had to be more than a one-off activity session, where a programme of physical activity was delivered through scheduled sessions, educational resources, or both. Comparison/control cohorts included those with no physical activity intervention, normal daily activity and individuals without Type 1 diabetes. The outcomes of interest were physiological, psychological, behavioural and social, and study designs could be randomized or non-randomized. Articles had to

have been peer-reviewed and published in the English language. There was no limitation on the year of publication or length of follow-up.

Search methods

The following databases were searched using the search strategy shown in Fig. 1: CINAHL Plus; the Cochrane Library; EMBASE; MEDLINE; PsycINFO; SCOPUS; Sport-Discus; and Web of Science (search terms are provided in Appendix S1). Searches were conducted between October 2012 and December 2012. The reference lists of review articles and included studies were searched by hand.

Two of the authors (H.Q. and R.T.) independently reviewed abstracts of potentially relevant articles derived from the search. Abstracts not fitting the inclusion criteria were excluded. If the abstract suggested potential eligibility, the full article was retrieved. Inclusion was based on agreement by the authors and reasons for exclusion were recorded. Disagreements were presented to a third author (H.B.), who made the final decision to include or exclude the article.

Data extraction and study quality

Two of the authors (H.Q. and R.T.) independently extracted the data, and variations in data extraction were resolved through discussion. The authors of the included studies were contacted via email for clarification of study methods or data wherever there was insufficient detail reported (17 authors were contacted, 10 authors provided information). The methodological quality of articles was assessed independently by the reviewers, based on the quality criteria specified by the Cochrane Collaboration [14] and Critical Appraisal Skills Programme checklists [15]. Alterations were made to the Cochrane Collaboration risk of bias tool to accommodate the non-randomized studies included.

Measures of treatment effect

In the present review, a control group was defined as participants with Type 1 diabetes who did not participate in the intervention. A comparison group was defined as participants without Type 1 diabetes who participated in the intervention. A randomized controlled trial refers to studies including a control group with Type 1 diabetes, in which participants were randomized to their group at the beginning. A non-randomized study refers to a controlled before-and-after study, with a control or comparison group (no randomization), or a prospective cohort study (no control or comparison group).

Wherever possible, findings from randomized or non-randomized studies with a control group were synthesized in the meta-analyses using review manager software (REVMAN 5.2, Cochrane Collaboration, Oxford, UK). The

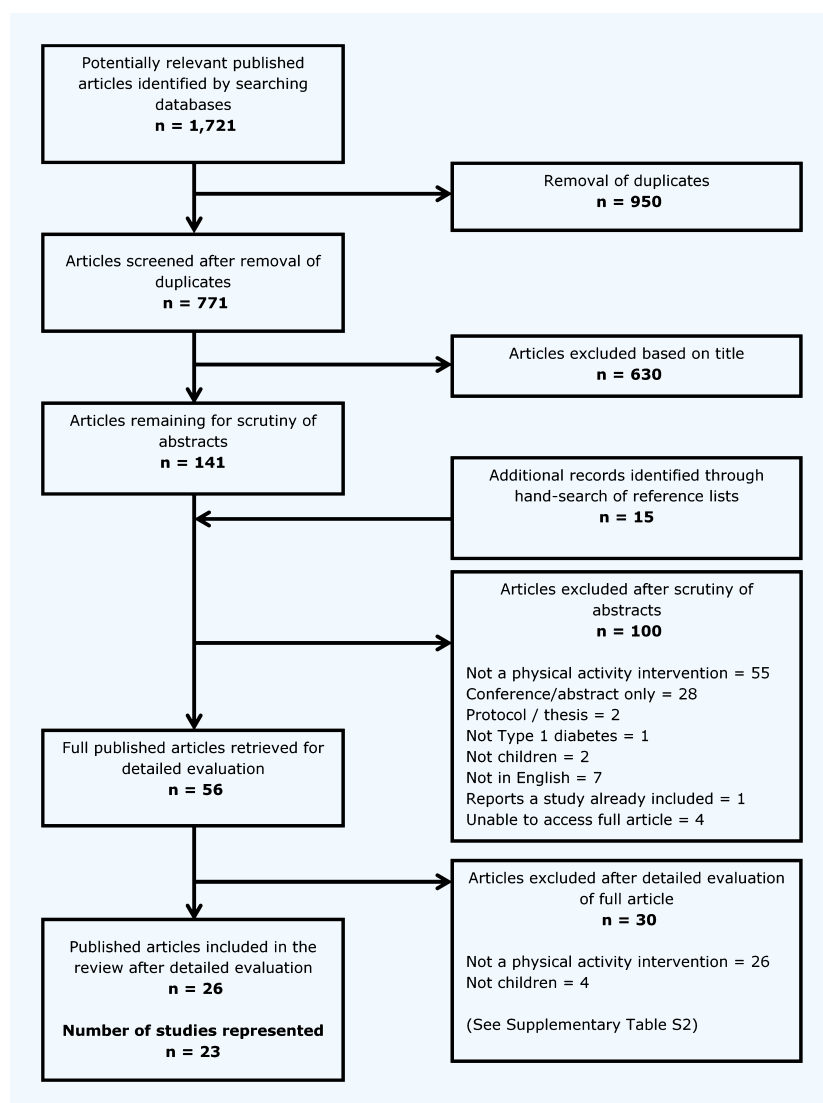


FIGURE 1 Flow chart showing article selection strategy, including reasons for exclusion according to the PRISMA guidelines.

effect size for the intervention was calculated based on the difference in change of a measurement before and after the intervention between an intervention (exercise) and control (no exercise) group. Standardized mean difference was used as the summary statistic for the overall effect size, with the associated 95% CIs. Studies measuring outcomes with different units of measurement were not synthesized in the meta-analyses, with the exception of glycated haemoglobin, where measurements of HbA_{1c} or HbA₁ differ only for a constant multiplier. All studies under review expressed glycated haemoglobin as HbA₁ or HbA_{1c} (Diabetes Control and Complications Trial-aligned percentages).

Assessment of heterogeneity and publication bias

Heterogeneity between studies was determined using the chi-squared test. Random-effects analysis was performed

when significant heterogeneity was present. We intended to assess publication bias using funnel plots.

Subgroup and sensitivity analysis

Subgroup analyses for activity type, intensity and frequency, duration of intervention and supervision were planned, depending on the availability of data. Sensitivity analyses were planned to explore the influence of different factors on effect size by repeating analyses as follows: 1) excluding studies with imputed values; 2) excluding non-randomized studies; and 3) excluding studies rated as having a high risk of bias.

Results

The search identified 1721 records, and 56 full articles met the inclusion criteria for further examination (Fig. 1). In all,

30 articles were excluded and the reasons reported (Table S1). The remaining 26 articles (representing 23 studies) were selected for review. Studies included 10 randomized and 16 non-randomized studies (nine controlled before-and-after studies, seven prospective cohort studies), published between 1964 [16,17] and 2012 [10,18]. Studies were conducted in 15 different countries; none were UK-based (Table S2).

Participants

Sample sizes ranged between 10 [19] and 196 [20], with a total of 756 participants, 661 with Type 1 diabetes. Six non-randomized studies had a comparison group of participants without Type 1 diabetes [16,17,21–24]. Three non-randomized studies had a control group with Type 1 diabetes who did not participate in the intervention [25–27]. All randomized studies involved participants with Type 1 diabetes only, with the exception of one involving participants with and without diabetes randomized to either an intervention or a control group (i.e. four groups) [10]. The mean \pm SD age of participants with diabetes ranged from 8.5 ± 0.57 to 17 ± 1.2 years [21, 28]. Most studies included both sexes, except five studies that included boys only [16,17,21,24,25] and three that included girls only [22,23,29].

Interventions

Recruitment and setting

Most studies recruited participants via diabetes clinics, eight studies did not report the location of recruitment [16,17,21–26,30] and one study recruited via a diabetes summer camp [31]. Only one study reported the recruitment method (i.e. invitation [31]). A total of 18 interventions were delivered under the supervision of an athletics coach or trainer, physiotherapists, physicians or study personnel. Supervised interventions were delivered at a hospital [18,20,30], swimming pool [22], gymnasium [25], sports centre [32], college [26], performance laboratory [21,24] or outdoors [25]. Five interventions were unsupervised, involving pedometers [33], video programmes [19,27] and personalized activities [8,34]. Three interventions included both unsupervised and supervised sessions [26,29,35].

Duration

The length of interventions ranged from 2 [31] to 39 weeks [10]. The modal duration of intervention was 12 weeks [18,19,21,24,27,28,33,36,37]. Two interventions lasted < 12 weeks [30, 31] and 15 lasted > 12 weeks. All studies used a single post-intervention follow-up, except two with a maintenance follow-up; Ruzic *et al.* [31] measured HbA_{1c} and blood glucose levels at 10 days and 2 months after cessation of a summer camp intervention, and Wong *et al.*

[27] measured HbA_{1c} levels, peak oxygen uptake and perceived exertion at 6, 9 and 12 months after a home-based aerobic activity intervention.

Time and frequency

Activity sessions ranged between 30 min [27,28,30,32] and 120 min [29]. Sessions of at least 60 min occurred in 13 studies and there was a tendency for the sessions lasting < 60 min to be published before 1990 [19,28,30,32,36]. The number of sessions varied between 1 and 5 days per week, except one study where activities took place three times per day during a 2-week diabetes summer camp [31]. Two studies [20,25] had two active intervention groups, one low and one high frequency activity (e.g. twice and 4 days a week [25]). Home-based interventions required an accumulation of activity to meet a goal (e.g. 10 000 steps per day [33]).

Type of activity

Interventions were aerobic [17,19,22,24,25,27,28,30–32,34,36–38] or a combination of aerobic and strengthening activity [10,18,20,21,29,35,39]. Single aerobic exercises included running and walking [25,37], swimming [22,23] and dance [19,27,36]. Other interventions varied the activities and included circuit training, cycling, skipping, ball and team games. Strengthening exercises included weight-bearing and resistance exercises such as weight training [20,21,39], jumping [10] and sprinting [35]. Balance and flexibility activity, such as Pilates [18] were also included. In four studies, the programme of activity was personalized to allow participants to choose the type of activity and when the activity was performed [8,19,33,34]. Ten interventions involved progression in the length [27] or intensity [16,17,20,21,24,25,29,37,39] of the activity over time.

In studies with a non-intervention control group, participants were instructed to continue with normal daily activity [10,18,20,25–29,33,36,39], except one group who participated in non-physical activities [38] and another who were given physical activity guidelines (20–60 min, 3–6 days per week)[30]. Wong *et al.* [27] reported that five control participants were reassigned to a group of ‘self-directed exercisers’, although no significant differences in outcomes were reported for this group.

Intensity of activity

The intensity of activity was reported in 19 studies [8,10,19–25,27–29,31,32,34,36–39]. Aerobic activities were performed at light (55–64% maximum heart rate) [24,31], moderate-to-vigorous (65–74% maximum heart rate) [8,10,21–23,34,35,38,39], vigorous (75–90% maximum heart rate) [19,28,29,36,37], or a combination of moderate activities and vigorous activities [20]. Strengthening activities were performed based on one repetition maximum values [21,39], 10 repetition maximum values and 85–95% maximum heart rate [20].

Diet or insulin advice

Seven studies provided the intervention group with advice about diet or insulin regimen [19, 21, 29–32, 36, 37]. In five of these [19,31,32,36,37], participants were given specific advice, for example ‘add 30 to 40 g of carbohydrate 30 minutes before exercising’ [37], but the advice differed across studies. In three studies, participants were asked to continue their usual diet and insulin regimen [21,29,30]. Five studies monitored diet [17,28,30,31,36], but did not attempt to change diet, none of which reported any significant change in calorie intake. One study, conducted during a diabetes summer camp, provided a controlled diet and individualized changes to insulin dosages in participants [31].

Theoretical underpinning

One study reported that the intervention had a theoretical underpinning [8] (Social Cognitive Theory and Family Systems Theory). Newton *et al.* [33] used text messaging as a motivational tool, but did not refer to motivation theory.

Effect of interventions

Physical activity and fitness

Four studies measured physical activity before and after the intervention in intervention and control or comparison groups [8,29,33,34]. One study, reported in two articles [8,34] measured intensity and frequency of activity during the intervention with accelerometers, and baseline level of physical activity with a 7-day physical activity recall questionnaire. Heyman *et al.* [29] also used a self-report physical activity questionnaire to estimate the total weekly physical activity attributed to the intervention. Newton *et al.* [33] used step-count as well as a self-reported physical activity questionnaire.

Faulkner *et al.* [34] and Michaliszyn and Faulkner [8] found that adolescents adhered to 60 min of moderate-to-vigorous activity per day for a mean of 45.5% of days during which an accelerometer was worn for the 16-week home-based aerobic activity intervention; spending a daily average of 10 h in sedentary activity and 42 min in moderate-to-vigorous activity. Heyman *et al.* [29] reported a significant increase in total weekly physical activity in the intervention group, and a significant difference between the intervention and control group. Newton *et al.* [33] found no significant difference in change in physical activity in adolescents after a 12-week pedometer intervention.

A total of 19 studies measured changes in various markers of fitness, 14 of which reported a beneficial effect of the intervention on some area of fitness, such as improved cardiovascular fitness [8,16,21,22,24,28,32,34–38]. Three studies (66 participants) were pooled in a meta-analysis which found a nonsignificant effect of physical activity on maximal oxygen uptake (VO₂ max) [standardized mean difference 0.24; $P = 0.33$ (Fig. 2a)]. Four studies did not measure any

marker of physical fitness or physical activity as an outcome [10,20,25,31].

Glycated haemoglobin

In 20 studies HbA_{1c} was measured, 11 of which were appropriate for meta-analysis. A random-effects model meta-analysis (11 studies, 345 participants) produced a standardized mean difference of -0.52 (95% CI -0.97 to -0.07), which was significantly different from 0 ($Z = 2.29$; $P = 0.02$). Effect sizes in nine of the 11 studies in the meta-analysis were < 0 (Fig. 2b), although there was significant heterogeneity between studies (chi square = 33.94, $P = 0.0002$). Sensitivity analyses, excluding studies with imputed standard deviation values and non-randomized studies, resulted in decreases in magnitude of the overall effect. After excluding studies that were rated as having a high risk of bias [26], the magnitude of the overall effect was increased (standardized mean difference -0.62, 95% CI -1.07 to -0.17; $P = 0.007$).

Of the studies that could not be pooled in the meta-analysis, two reported significant decreases in HbA_{1c} levels after the physical activity intervention [8,23] and six reported no significant change in HbA_{1c} [21,24,32,33,37,39]. Ruzic *et al.* [31] reported a significant initial decrease in HbA_{1c} level 10 days after the intervention, followed by a significant increase in HbA_{1c} 2 months later.

Daily insulin dose

Nine studies measured daily insulin dose before and after the physical activity intervention [18,20,23,24,26,30,32,33,39]. Three studies (174 participants) had data appropriate for meta-analysis. There was no overall difference in daily insulin dose [standardized mean difference -0.78, $P = 0.07$ (Fig. 2c)]. In studies where data could not be pooled in the meta-analysis, three demonstrated decreases in insulin dose among participants in the intervention group [23,30,39], although one found a reduction in short-acting insulin only [23]. Two studies reported no significant change in daily insulin dose [24,32,33].

Lipid profile

Serum lipids were measured in 11 studies [8,18,20–22,24,25,29,30,32]. Triglycerides, total cholesterol, HDL cholesterol and LDL cholesterol were reported. Five studies reporting triglycerides, total cholesterol and HDL cholesterol, and four studies reporting LDL cholesterol were appropriate for meta-analysis.

A random-effects model meta-analysis for triglycerides (five studies, 206 participants) produced a standardized mean difference of -0.70 (95% CI -1.25 to -0.14), which was significantly different from 0 ($Z = 2.45$; $P = 0.01$). Effect sizes

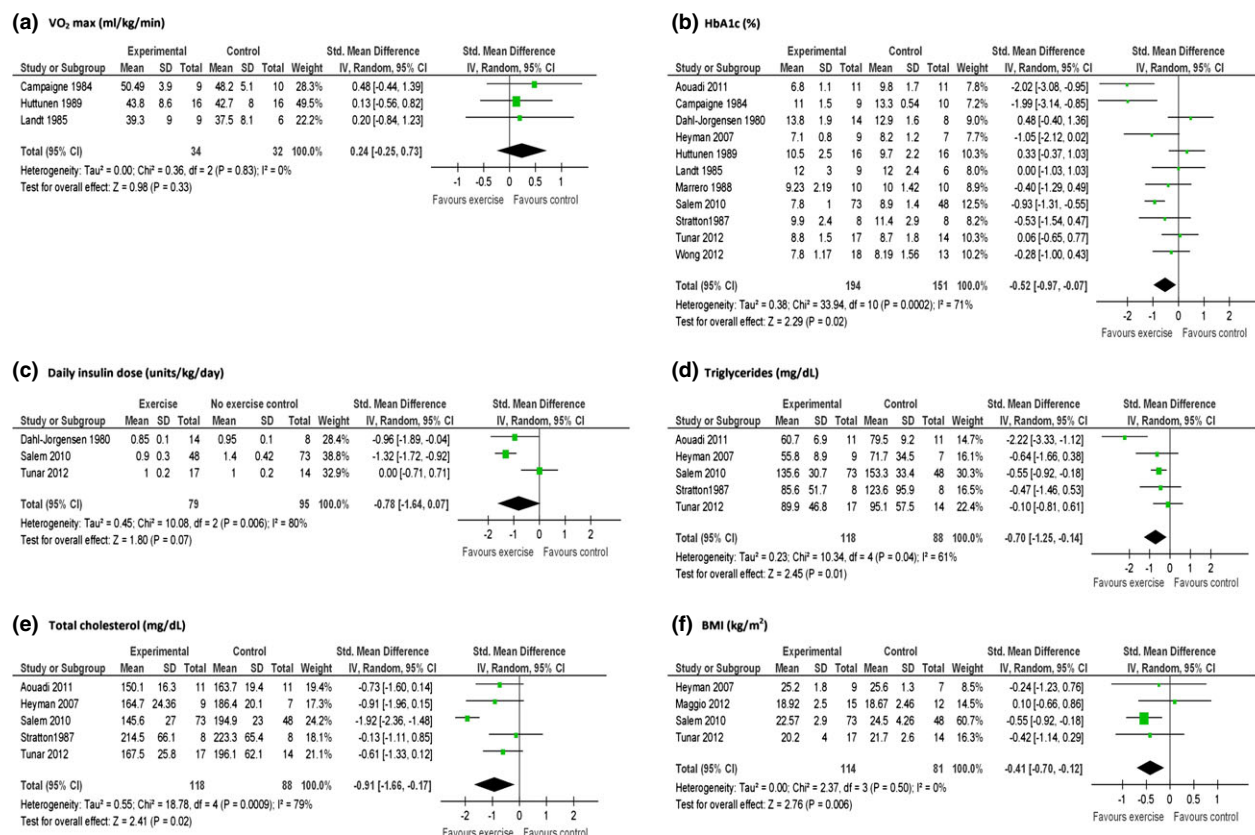


FIGURE 2 (a–f) Forest plots showing estimates of the size of change in outcomes after a physical activity intervention. (a) VO₂ max, (b) HbA_{1c}, (c) Daily insulin dose, (d) Triglycerides, (e) Total cholesterol and (f) BMI.

in all five of the studies included in the analysis were < 0 (Fig. 2d), although there was significant heterogeneity between studies (chi square = 10.34; $P = 0.04$). A random-effects model meta-analysis for total cholesterol (five studies, 206 participants) produced a standardized mean difference of -0.91 (95% CI -1.66 to -0.17), which was significantly different from 0 ($Z = 2.41$; $P = 0.02$). Effect sizes in all five of the studies included in the analysis were < 0 (Fig. 2e), although there was significant heterogeneity between studies (chi square = 18.78; $P = 0.0009$). There was no significant effect of physical activity on HDL cholesterol (standardized mean difference 0.36; $P = 0.49$) or LDL cholesterol (standardized mean difference -0.54 ; $P = 0.21$). A sensitivity analysis excluding non-randomized studies did not change the inference from the meta-analyses.

Lipid data from four studies could not be pooled in the meta-analysis, Michaliszyn and Faulkner [8] reported that time spent in light, moderate and moderate-to-vigorous activity was associated with decreases in total cholesterol, LDL cholesterol and triglycerides. Mosher *et al.* [21] found significant increases in HDL cholesterol and decreases in LDL cholesterol in adolescent males with and without Type 1 diabetes. Woo *et al.* [24] found no significant changes in total cholesterol or HDL cholesterol in boys with and without diabetes. Sideravičiūtė *et al.* [22] found no significant changes

in lipid profile in adolescent girls with Type 1 diabetes after the swimming intervention, whilst HDL cholesterol significantly increased in girls without diabetes.

Body composition

Nine studies measured BMI [10,18,20,22,24,29,33,35,39]. A random-effects model meta-analysis (four studies, 195 participants) produced a standardized mean difference of -0.41 (95% CI -0.70 to -0.12), which was significantly different from 0 ($Z = 2.76$; $P = 0.006$). Effect sizes in three of the four studies included in the analysis were < 0 (Fig. 2f), with no significant heterogeneity between studies (chi square = 2.37; $P = 0.50$).

Results from five studies could not be pooled in the meta-analysis. Salem *et al.* [20] reported a significant decrease in BMI in both groups of children who performed physical activity sessions once and three times per week, and the reduction was greater in those who participated three times a week. Sideravičiūtė *et al.* (2006) observed a higher BMI in adolescent girls with Type 1 diabetes compared with girls without diabetes before and after a swimming programme. The remaining studies found no significant change in BMI [24,27,39].

Nine studies measured body weight [10,16,21,22,29,30,32,35,37], three of which reported significant increases

in body weight after physical activity [16,22,32]. Four studies reported waist circumference [20,29,35,39]. Salem *et al.* [20] reported a significant decrease in waist circumference in children and the greatest reduction in those who participated three times a week compared with once a week. Six studies measured fat mass [8,21,22,24,29,39]; three using bioimpedance techniques [8,24,39] and three computing fat mass from skinfold measures [21,22,29]. Decreased fat-mass was observed in two studies after the intervention [21,22]. Three studies reported fat-free mass using bioimpedance [8,39] or computed it from skinfold measures [29]. Fat-free mass was found to increase in the physical activity group [29] and to be positively associated with time spent in moderate, vigorous and moderate-to-vigorous physical activity [8]. Three studies reported lean body mass [10,21,36]. Mosher *et al.* [21] reported that adolescent males with Type 1 diabetes gained lean body mass after 12 weeks of circuit training three times a week. Two studies reported no significant changes in skinfold thickness [21,30].

Quality of life

Quality of life was measured in four studies using three different measures [29,33,34,39]. D'hooge *et al.* [39] and Faulkner *et al.* [34] found no significant changes in quality of life after the intervention. Heyman *et al.* [29] reported improvement in 'satisfaction with diabetes' in the intervention group. Newton *et al.* [33] found quality-of-life scores to be below the normative range at baseline in adolescents with Type 1 diabetes, with no significant changes after the 12-week pedometer intervention.

Exercise perceptions

Faulkner *et al.* [34] measured perceptions of exercise using scales for perceived self-efficacy, perceived benefits of action and perceived barriers to action [40]. Faulkner *et al.* also used the exercise subscale of the Diabetes Social Support Questionnaire-family version [41]. They reported that children's perception of normative family support for exercise increased significantly between before and after the intervention.

Other effects of interventions

Some physiological health indicators were explored in isolation and included serum apolipoproteins, lipoprotein (a), leptin and adiponectin [29], bone mineral density [10], endothelial function [35] and oxidative stress [24] (Table S3).

Fidelity and adherence

Fidelity of the intervention, in terms of the delivery of the programme content, was not reported in any article. Adherence to the physical activity programme was reported as a

percentage in five articles [8,20,29,33,34] and ranged between 52 and 100%. Attendance at activity sessions was reported in four articles [10,19,37,39]. After email contact, two authors provided further details about adherence [21,35]. In three studies, the rate of adherence or attendance was not reported, but instead participants were required to attain a pre-specified percentage of attendance, which differed in each study [21,27,28]. A total of 13 articles did not report adherence or attendance. During supervised activity sessions, adherence was monitored via heart rate monitoring [20,21,29]. In the home-based interventions, methods of monitoring adherence included telephone interviews and activity logs [27], measurement via accelerometers [8,34], text messages and daily step count charts [33], post-intervention interviews [19] and an online log [35].

Adverse effects

The occurrence of hypoglycaemia was reported in nine studies [10,19–21,25,28,31,34,36,37,39], two of which reported that hypoglycaemia did not occur [10,36]. Hypoglycaemic episodes were mild and varied in frequency, ranging from no episodes to at least one episode in most participants, either during or after activity [19]. After email contact, Heyman *et al.* [29] reported 17 mild episodes of hypoglycaemia. No other adverse effects of physical activity were reported.

Risk of bias

Most non-randomized studies were judged to have an unclear risk of bias and three studies were judged to have a high risk of bias. One study was rated as having an unclear risk for 'selective reporting bias' as changes in the control group were not reported [25], although the author provided the control group data when contacted. One study was rated as having a high risk of 'measurement bias' for a lack of detail in reporting of measurement and outcomes and potential bias in the way HbA_{1c} was measured [26]. The studies by Larsson *et al.* [16,17] were rated as having a high risk of selection bias because of unrepresentative intervention and control group samples (i.e. boys with an interest in sport and their friends who became the control group; Table S4).

A total of 10 studies were described by the authors as having randomized designs, but only two reported the method of randomization or allocation concealment; for example, closed envelopes [10,39]. After email contact, four authors reported having used procedures such as drawing lots [29], closed envelope [20], computer randomization [28] and a systematic sampling method [18].

Publication bias

Funnel plot asymmetry was assessed for the HbA_{1c} outcome. Visual assessment of the funnel plot indicated bias (Fig. S1). This may imply publication bias, but might reflect the

methodological heterogeneity between studies. There were inadequate numbers of studies in the other meta-analyses to properly assess funnel plots.

Subgroup analyses

Subgroup analyses were performed for the HbA_{1c} outcome when sufficient data were available (Fig. S2). Including only the studies with physical activity performed ≥ 3 days per week (eight studies, 275 participants), the effect size remained significant and increased (standardized mean difference -0.70, 95% CI -1.18 to -0.22; $P = 0.004$). When only studies with physical activity on < 3 days per week were included (five studies, 215 participants), there was no significant effect on HbA_{1c}. Based on subgroup analyses, the standardized mean difference for physical activity on ≥ 3 days per week was 0.18 greater than for all studies combined, which may indicate the minimum dosage of physical activity required to produce a clinical benefit for young people with Type 1 diabetes.

Subgroup analyses for interventions < 12 weeks (six studies, 132 participants) and > 12 weeks (five studies, 213 participants) in duration, and interventions with diet or insulin advice (four studies, 67 participants) and without diet or insulin advice (seven studies, 278 participants), did not reach statistical significance.

Discussion

Most studies found significant improvement in at least one health outcome after a physical activity intervention, with only two studies observing no statistically significant health outcomes [27,33]. A broad range of outcomes were reported, making direct comparison of intervention effects problematic. Nevertheless, meta-analyses identified significant effects of physical activity on reductions in HbA_{1c}, BMI, triglycerides and total cholesterol, which reinforce the importance of a physical activity in the clinical management of diabetes to delay or reduce the risk of microvascular complications [42] and cardiovascular disease.

The moderate-sized effect of physical activity intervention on HbA_{1c} could be clinically significant for young people with Type 1 diabetes. Assuming the SD for HbA_{1c} of 16.4 mmol/mol (1.5%) observed in the literature [43], the effect size from this meta-analysis (-0.52) would give a reduction in HbA_{1c} of 8.5 mmol/mol (0.78%). The large and moderate-to-large effect sizes of physical activity on total cholesterol and triglycerides found in the present review may have clinical relevance for improving lipid profiles in young people with diabetes who are known to have abnormal lipid levels compared with those without diabetes [44]. Findings should be interpreted with caution as some level of bias was present in all included studies, with the additional unknown confounding effect of diet and insulin adjustments in children's treatment practices.

It is surprising that just four studies measured physical activity as an outcome of the intervention. Studies were more likely to report changes in physical fitness, but four studies failed to measure either physical fitness or physical activity. This makes it difficult to show whether any health benefits found were related to change in physical activity, or to determine the dosage of physical activity required to bring about health benefits. Furthermore, measures of physical activity often relied upon self-reported recall rather than objective measures. Nevertheless, these studies suggest that physical activity interventions improve cardiovascular fitness and have the potential to increase physical activity levels.

The effect of interventions on psychological outcomes

Only four studies assessed the psychological impact of physical activity, each assessing quality of life and one reporting improvement in this psychological health outcome. Quality of life is known to be poorer in young people with Type 1 diabetes than in their peers without diabetes [45]. In one study [39], participants had shown good quality of life at the outset, which may have reduced the power of the study to detect a difference. There is a paucity of research exploring the relationship between physical activity and psychological outcomes in young people with diabetes.

Characteristics of interventions

Intervention characteristics were diverse. There was variation in total duration of the intervention, length of each session, type of activity performed, intensity of activity, delivery setting and supervision. No intervention delivered or accrued the UK guideline of 60 min of moderate-to-vigorous physical activity per day, although many were conducted before the release of physical activity guidelines for children and none were conducted in the UK.

Of those interventions involving a home-based component, only one study reported using influential factors in the home environment, by asking a parent to adopt an active lifestyle and thus provide their child with an active role model [8,34]. In the studies utilizing parental influence, the level of parental physical activity was unknown, which limits the conclusions that can be drawn about the influence of parental role models on physical activity. It is well established that parents are important correlates of physical activity in young people without diabetes, especially as active role models and sources of emotional and logistical support [46]; parental influence on physical activity participation in children with Type 1 diabetes is therefore an area for future research.

Health behaviour change theory can improve the development and delivery of interventions, [47] and theoretically driven physical activity interventions produce larger effect sizes [48]. Only two studies in the present review reported any theoretical underpinning.

The assessment of maintenance is particularly important when considering behaviour change interventions and yet only two studies in the present review implemented a maintenance follow-up [27,31], one of which found that lowered HbA_{1c} levels after a 2-week physical activity intervention were not sustained at a 2-month follow-up [31]. In children, sustained behaviour change may be more desirable than temporary behaviour change [49]. For those with Type 1 diabetes, sustained increases in physical activity will potentially benefit insulin requirement, weight management and blood glucose control, and help towards delaying the onset of cardiovascular disease.

Adherence rates and adverse events

Few studies reported adherence rates, and there was a tendency to report attendance at sessions rather than adherence to the activity programme. Those that did report adherence showed a good, if diverse, range of adherence (52–100%). This is similar to rates of adherence in physical activity interventions in young people without diabetes [50], although the reporting of intervention exposure and adherence seems to be a common weakness in studies across the population [51].

In interventions with unsupervised components, it is necessary that compliance to the programme is monitored. When participants choose their preferred activity, engagement may be enhanced through choice and independence, which have been found to be facilitators of physical activity participation in young people [52]; however, monitoring techniques (e.g. activity logs) have not been evaluated. It is difficult to draw firm conclusions about the effects of interventions on health outcomes when it is unclear whether participants fully adhered to the programme of activity.

It is encouraging that no severe episodes of hypoglycaemia were reported, since studies indicate a fear of hypoglycaemia in young people with Type 1 diabetes and their parents [53]; however, anxiety about hypoglycaemia can exist even in those with no history of severe hypoglycaemia [53], which emphasizes that psychological factors associated with physical activity for young people with Type 1 diabetes need further exploration.

Recommendations for future research

Future research should not only focus on clinical outcomes but explore the potential behavioural and psychological benefits of physical activity for young people with diabetes. Interventions should be theory-driven to include elements known to be associated with behaviour change and help explain *how* interventions bring about change. Interventions should be designed to encourage children and young people to be physically active for at least 60 min/day. Maintenance follow-up data are required to explore whether changes in

important health outcomes are sustained over time. Intervention studies should monitor adherence to the programme of activity and would benefit from evaluating the success of adherence strategies.

Potential biases in the review process

The inclusion of non-randomized studies increases the risk of bias in the present review, but it can be argued that the knowledge gained provides a more valuable insight into existing interventions and the potential health-related outcomes of physical activity, which warrants their inclusion and credibility.

Conclusions

The present review suggests that physical activity interventions can have a range of health benefits for children and young people with Type 1 diabetes. These findings are clinically important with regard to diabetes management and delaying the premature onset of complications, such as cardiovascular disease. Despite promising findings, existing interventions have not used the psychological theory of health behaviour change or determined the long-term sustainability of positive health outcomes. Heterogeneity in study design, methods and reporting remains a barrier to fully understanding the influence of physical activity on health outcomes in young people with Type 1 diabetes, therefore, more clarification is required to understand which elements of physical activity interventions are most effective for young people with Type 1 diabetes, and how changes in physical activity might occur.

Funding sources

This review was conducted as part of a PhD for H.Q. funded by a DTA studentship from the University of Nottingham (School of Health Sciences and Division of Psychiatry and Applied Psychology NIHR CLAHRC).

Competing interests

None declared.

References

- 1 Soedamah-Muthu SS, Fuller JH, Mulnier HE, Raleigh VS, Lawrenson RA, Colhoun HM. High Risk of Cardiovascular Disease in Patients With Type 1 Diabetes in the U.K.: A cohort study using the General Practice Research Database. *Diabetes Care* 2006; 29: 798–804.
- 2 Babar GS, Zidan H, Widlansky ME, Das E, Hoffmann RG, Daoud M *et al.* Impaired Endothelial Function in Preadolescent Children With Type 1 Diabetes. *Diabetes Care*. 2011; 34: 681–685.
- 3 National Institute for Health and Clinical Excellence (NICE). Type 1 diabetes in children, young people and adults: NICE guideline

- 2004 26th November 2012. Available from: <http://www.nice.org.uk/nicemedia/live/10944/29390/29390.pdf>.
- 4 Department of Health. *Start active, stay active: a report on physical activity from the four home countries' Chief Medical Officers*, 2011. Available at http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_128209 Last accessed 11 July 2011.
 - 5 Edmunds S, Roche D, Stratton G, Wallymahmed K, Glenn SM. Physical activity and psychological well-being in children with Type 1 diabetes. *Psychol Health Med* 2007; **12**: 353–363.
 - 6 Department of Health. *At Least Five a Week. Evidence on the Impact of Physical Activity and Its Relationship to Health. A report from the Chief Medical Office*. London: Department of Health, 2004.
 - 7 Craig R, Mindell J, Hirani V. *Health survey for England 2008: physical activity and fitness*, 2008. Available at <http://www.hscic.gov.uk/catalogue/PUB00430/heal-surv-phys-acti-fitt-eng-2008-rep-v1.pdf> Last accessed 11 July 2011.
 - 8 Michaliszyn SF, Faulkner MS. Physical activity and sedentary behavior in adolescents with type 1 diabetes. *Res Nurs Health* 2010; **33**: 441–449.
 - 9 Sundberg F, Forsander G, Fasth A, Ekelund U. Children younger than 7 years with type 1 diabetes are less physically active than healthy controls. *Acta Paediatr* 2012; **101**: 1164–1169.
 - 10 Maggio ABR, Rizzoli R, Marchand LM, Ferrari S, Beghetti M, Farpour-Lambert NJ. Physical activity increases bone mineral density in children with type 1 diabetes. *Med Sci Sports Exerc* 2012; **44**: 1206–1211.
 - 11 Avery L, Flynn D, van Wersch A, Snihotta FF, Trenell MI. Changing Physical Activity Behavior in Type 2 Diabetes: A systematic review and meta-analysis of behavioral interventions. *Diabetes Care* 2012; **35**: 2681–2689.
 - 12 MacMillan F, Kirk A, Mutrie N, Matthews L, Robertson K, Saunders DH. A systematic review of physical activity and sedentary behavior intervention studies in youth with type 1 diabetes: study characteristics, intervention design, and efficacy. *Pediatr Diabetes* 2014; **15**: 175–189.
 - 13 Kennedy A, Nirantharakumar K, Chimen M, Pang TT, Hemming K, Andrews RC *et al*. Does Exercise Improve Glycaemic Control in Type 1 Diabetes? A Systematic Review and Meta-Analysis. *PLoS One* 2013; **8**: e58861.
 - 14 Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; **343**: d5928.
 - 15 Critical Appraisal Skills Programme (CASP). *Critical Appraisal Skills Programme: making sense of evidence about clinical effectiveness: 12 questions to help you make sense of cohort study*. Better Value Healthcare, 2010. Available at: http://www.casp-uk.net/wp-content/uploads/2011/11/CASP_Cohort_Appraisal_Checklist_14oct10.pdf. Last accessed 1 April 2013.
 - 16 Larsson Y, Persson B, Sterky G, Thorén C. Functional adaptation to rigorous training and exercise in diabetic and nondiabetic adolescents. *J Appl Physiol* 1964; **19**: 629–635.
 - 17 Larsson Y, Persson B, Sterky G, Thoren C. Effect of exercise on blood-lipids in juvenile diabetes. *Lancet* 1964; **1**: 350.
 - 18 Tunar M, Ozen S, Goksen D, Asar G, Bediz CS, Darcan S. The effects of Pilates on metabolic control and physical performance in adolescents with type 1 diabetes mellitus. *J Diabetes Complications* 2012; **26**: 348–351.
 - 19 Marrero DG, Fremion AS, Golden MP. Improving compliance with exercise in adolescents with insulin-dependent diabetes mellitus: results of a self-motivated home exercise program. *Pediatrics* 1988; **81**: 519–525.
 - 20 Salem M, AboElAsrar M, Elbarbary N, ElHilaly R, Refaat Y. Is exercise a therapeutic tool for improvement of cardiovascular risk factors in adolescents with type 1 diabetes mellitus? A randomised controlled trial. *Diabetol Metab Syndr* 2010; **2**: 47.
 - 21 Mosher PE, Nash MS, Perry AC, LaPerriere AR, Goldberg RB. Aerobic circuit exercise training: effect on adolescents with well-controlled insulin-dependent diabetes mellitus. *Arch Phys Med Rehabil* 1998; **79**: 652–657.
 - 22 Sideravičiūtė S, Gailiūnienė A, Visagurskienė K, Vizbaraitė D. The effect of long-term swimming program on body composition, aerobic capacity and blood lipids in 14–19-year aged healthy girls and girls with type 1 diabetes mellitus. *Medicina (Kaunas)* 2006; **42**: 661–666.
 - 23 Sideravičiūtė S, Gailiūnienė A, Visagurskienė K, Vizbaraitė D. The effect of long-term swimming program on glycemia control in 14–19-year aged healthy girls and girls with type 1 diabetes mellitus. *Medicina (Kaunas)* 2006; **42**: 513–518.
 - 24 Woo J, Yeo N, Shin K, Lee HJ, Yoo J, Kang S. Antioxidant enzyme activities and DNA damage in children with type 1 diabetes mellitus after 12 weeks of exercise. *Acta Paediatr* 2010; **99**: 1263–1268.
 - 25 Aouadi R, Khalifa R, Aouidet A, Ben MA, Ben RM, Mdini F *et al*. Aerobic training programs and glycemic control in diabetic children in relation to exercise frequency. *J Sports Med Phys Fitness* 2011; **51**: 393.
 - 26 Dahl-Jorgensen K, Meen H, Hanssen KF, Aagaas O. The effect of exercise on diabetic control and hemoglobin A1c (HbA1c) in children. *Acta Paediatr* 1980; **69**: 53–56.
 - 27 Wong CH, Chiang YC, Wai JP, Lo FS, Yeh CH, Chung SC *et al*. Effects of a home-based aerobic exercise programme in children with type 1 diabetes mellitus. *J Clin Nurs* 2011; **20**: 681–691.
 - 28 Campaigne BN, Gilliam TB, Spencer ML, Lampman RM, Schork MA. Effects of a physical-activity program on metabolic control and cardiovascular fitness in children with insulin-dependent diabetes-mellitus. *Diabetes Care* 1984; **7**: 57–62.
 - 29 Heyman E, Toutain C, Delamarche P, Berthon P, Briard D, Youssef H *et al*. Exercise training and cardiovascular risk factors in type 1 diabetic adolescent girls. *Pediatr Exerc Sci* 2007; **19**: 408.
 - 30 Stratton R, Wilson DP, Endres RK, Goldstein DE. Improved glycemic control after supervised 8-wk exercise program in insulin-dependent diabetic adolescents. *Diabetes Care* 1987; **10**: 589–593.
 - 31 Ruzic L, Sporis G, Matkovic BR. High volume-low intensity exercise camp and glycemic control in diabetic children. *J Paediatr Child Health* 2008; **44**: 122–128.
 - 32 Baevre H, Sovik O, Wisnes A, Heiervang E. Metabolic responses to physical training in young insulin-dependent diabetics. *Scand J Clin Lab Invest* 1985; **45**: 109–114.
 - 33 Newton KH, Wiltshire EJ, Elley CR. Pedometers and Text Messaging to Increase Physical Activity Randomized controlled trial of adolescents with type 1 diabetes. *Diabetes Care* 2009; **32**: 813–815.
 - 34 Faulkner MS, Michaliszyn SF, Hepworth JT. A personalized approach to exercise promotion in adolescents with type 1 diabetes. *Pediatr Diabetes* 2010; **11**: 166–174.
 - 35 Seeger JP, Thijssen DH, Noordam K, Cranen ME, Hopman MT, Nijhuis-van der Sanden MW. Exercise training improves physical fitness and vascular function in children with type 1 diabetes. *Diabetes Obes Metab* 2011; **13**: 382–384.
 - 36 Landt KW, Campaigne BN, James FW, Sperling MA. Effects of exercise training on insulin sensitivity in adolescents with type I diabetes. *Diabetes Care* 1985; **8**: 461–465.
 - 37 Rowland TW, Swadba LA, Biggs DE, Burke EJ, Reiter EO. Glycemic control with physical training in insulin-dependent diabetes mellitus. *Arch Pediatr Adolesc Med* 1985; **139**: 307.
 - 38 Huttunen NP, Lankela SL, Knip M, Lautala P, Kaar ML, Laasonen K *et al*. Effect of once-a-week training program on physical fitness

- and metabolic control in children with IDDM. *Diabetes Care* 1989; 12: 737–740.
- 39 D'hooge R, Hellinckx T, Van Laethem C, Stegen S, De Schepper J, Van Aken S *et al.* Influence of combined aerobic and resistance training on metabolic control, cardiovascular fitness and quality of life in adolescents with type 1 diabetes: a randomized controlled trial. *Clin Rehabil* 2011; 25: 349–359.
 - 40 Pender NJ, Garcia AW, Ronis DL. Research Instruments 1995 [cited 2013 12th June]; Available at: <http://deepblue.lib.umich.edu/browse?type=author&order=ASC&rpp=20&value=Pender%2C+Nola+J>. Last accessed 1 June 2013.
 - 41 La Greca AM, Bearman KJ. The diabetes social support questionnaire-family version: Evaluating adolescents' diabetes-specific support from family members. *J Pediatr Psychol* 2002; 27: 665–676.
 - 42 Kriska AM, LaPorte RE, Patrick SL, Kuller LH, Orchard TJ. The association of physical activity and diabetic complications in individuals with insulin-dependent diabetes mellitus: The epidemiology of diabetes complications study—VII. *J Clin Epidemiol* 1991; 44: 1207–1214.
 - 43 Rosenbauer J, Dost A, Karges B, Hungele A, Stahl A, Bächle C *et al.* Improved Metabolic Control in Children and Adolescents With Type 1 Diabetes: A trend analysis using prospective multicenter data from Germany and Austria. *Diabetes Care* 2012; 35: 80–86.
 - 44 Guy J, Ogden L, Wadwa RP, Hamman RF, Mayer-Davis EJ, Liese AD *et al.* Lipid and Lipoprotein Profiles in Youth With and Without Type 1 Diabetes The SEARCH for Diabetes in Youth Case-Control Study. *Diabetes Care* 2009; 32: 416–420.
 - 45 Kalyva E, Malakonaki E, Eiser C, Mamoulakis D. Health-related quality of life (HRQoL) of children with type 1 diabetes mellitus (T1DM): self and parental perceptions. *Pediatr Diabetes* 2011; 12: 34–40.
 - 46 Lim C, Biddle SJ. Longitudinal and prospective studies of parental correlates of physical activity in young people: A systematic review. *Int J Sport Exerc Psychol* 2012; 10: 211–220.
 - 47 Michie S, Prestwich A. Are interventions theory-based? Development of a theory coding scheme. *Health Psychol* 2010; 29: 1–8.
 - 48 Webb TL, Joseph J, Yardley L, Michie S. Using the internet to promote health behavior change: a systematic review and meta-analysis of the impact of theoretical basis, use of behavior change techniques, and mode of delivery on efficacy. *J Med Internet Res* 2010; 12: e4.
 - 49 Jones RA, Sinn N, Campbell KJ, Hesketh K, Denney-Wilson E, Morgan PJ *et al.* The importance of long-term follow-up in child and adolescent obesity prevention interventions. *Int J Pediatr Obes* 2011; 6: 178–181.
 - 50 Ransdell LB, Taylor A, Oakland D, Schmidt J, Moyer-Mileur L, Shultz B. Daughters and mothers exercising together: effects of home-and community-based programs. *Med Sci Sports Exerc* 2003; 35: 286–296.
 - 51 Sluijs EMFv, McMinn AM, Griffin SJ. Effectiveness of interventions to promote physical activity in children and adolescents: systematic review of controlled trials. *BMJ* 2007; 335: 703.
 - 52 Brunton G, Harden A, Rees R, Kavanagh J, Oliver S, Oakley A. *Children and Physical Activity: A systematic review of barriers and facilitators – Executive Summary*. London: EPPI-Centre, Social Science Research Unit, Institute of Education, University of London, 2003.
 - 53 Johnson SR, Cooper MN, Davis EA, Jones TW. Hypoglycaemia, fear of hypoglycaemia and quality of life in children with Type 1 diabetes and their parents. *Diabet Med* 2013; 30: 1126–1131.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Key terms used in the database search.

Table S1. Reasons for exclusion table.

Table S2. Details of included studies.

Table S3. Study outcome measures table.

Table S4. Quality assessment summary tables.

Figure S1. Funnel plot testing for publication bias in the HbA_{1c} meta-analysis.

Figure S2. Subgroup analyses for HbA_{1c} outcomes.